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Specific influence of salts on the hydrolysis reaction rate of *p*-nitrophenyl anthranilate in binary acetonitrile–water solvents

Leta Danno Bayissa, Yoshihito Ohmae, Masashi Hojo *

Department of Chemistry, Faculty of Science, Kochi University, Akebono-cho, Kochi 780-8520, Japan

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ABSTRACT

The hydrolysis reaction rates of *p*-nitrophenyl anthranilate (*p*-NPA) have been surveyed in aqueous buffer solutions mixed with acetonitrile (MeCN) containing various salts at 50 ± 0.1 °C. Increase in pH of the buffer solution from 8.50 to 10.0 results in an increase of the hydrolysis rate constant [log (k/s^{-1})] in all solutions mixed with 0–75% (v/v) MeCN. The log (k/s^{-1}) values significantly decelerate as MeCN contents increase to about 50% (v/v). With further increment of MeCN contents, however, the reversal increases in log (k/s^{-1}) are observed. All the added salts significantly influence the hydrolysis rate in solutions containing the borate buffer of pH = 9.18. Alkali metal perchlorates ($LiClO_4$ and $NaClO_4$) cause the deceleration with increasing salt concentration. The presence of as low as 0.1 mol dm^{-3} of NaN_3 causes a three-fold acceleration, compared to the rate without the salt in no MeCN media. The rate acceleration by NaN_3 becomes gradually weaker as the MeCN contents increase. Contrastingly, the rate acceleration by Et_4NBr is enhanced with increasing MeCN contents. In 50% (v/v) MeCN solution, the acceleration in log (k/s^{-1}) caused by added salts is in the order of $NaN_3 > (n\text{-Bu})_4NBr \sim Et_4NBr > Et_4NCl$. The Arrhenius plots in the 50% (v/v) MeCN media without salts and with 0.20 mol dm^{-3} of $LiClO_4$, NaN_3 and Et_4NBr salts give the good linearity of high activation energy values in the temperature range of 35 to 60 ± 0.1 °C, suggesting that the hydrolysis reactions are just of temperature dependence. The whole results have been discussed in terms of changes in the water structure and/or activities of H_2O and OH^- in the presence of both the added organic solvent and salts, and also in terms of the nucleophilicity of anions from the added salts in the "modified" media.

1. Introduction

The *p*-nitrophenyl ester is known to be an active ester due to the strong electronegativity of the nitro group. This active ester, however, is well-tolerated by the aromatic amine group, which is a nucleophile, in *p*-nitrophenyl anthranilate (*p*-NPA). *p*-Nitrophenyl anthranilate has two different functional groups: an aryl amine that can react with free reducing glycans by reductive amination and an active *p*-nitrophenyl ester that can react with nucleophiles. This bifunctional linker has been used for preparing fluorescent neoglycoproteins from naturally occurring complex glycans [1]. It is worth noting that the linking property of this active ester, *p*-nitrophenyl anthranilate, under different conditions could be affected by its interaction with water.

Hydrolysis of an ester may occur through three pathways: base catalyzed, pH independent, and acid catalyzed reaction pathways [2]. These pathways are independent of each other as demonstrated by Hine [3]. El-Mallah et al. [4] have indicated that the rate of chemical reactions in solution can be influenced by two types of the solvent effects, *i.e.*, nonspecific and specific. Nonspecific solvent effects denote the electrostatic interaction of the solvent molecules with the ionic substances, whereas specific solvent effects denote the chemical interaction due to the presence of electron-donating and/or electron-accepting centers in the solvent molecules.

There is an increased interest in understanding the effects of reaction medium, of both pure solvents and binary mixtures on the rate and equilibrium constants of chemical and biochemical reactions [5–9]. Solvent effects on the kinetic studies of the hydrolysis of various esters have been reported [10–15]. The effects of acetonitrile–water mixtures on the hydrolysis of 4-nitrophenyl chloroformate and heptafluorobutyrate [16], bis(*p*-nitrophenyl) phosphate [17], *p*-nitrophenyl acetate, benzoate [18,19] and anthranilate [20] and oxazolinone [21,22] have been reported.

In addition to solvent effects, the presence of various salts also has been examined regarding their significant impact on reactions of organic compounds. In their report on the hydrolysis of organic compounds, Mabey and Mill [23] have indicated the effects of both solvent composition and added salts. The added salts can lead either to rate acceleration or deceleration, depending on the substrate, the specific salts, and their concentration.

There have been many experimental and computational approaches addressing the issue of water structure in the presence of added salts

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* Corresponding author. Tel.: +81 88 844 8306; fax: +81 88 844 8359.
E-mail address: mhojo@kochi-u.ac.jp (M. Hojo).

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and organic solvent mixtures, since water is a common solvent and many chemical reactions take place in water [24]. Disruption of the tetrahedral water structure in the presence of added salt and organic solvents has been reported [25,26]. We have proposed an innovative idea [27] that the properties of bulk water originate from the intermolecular hydrogen-bonded network among a huge number of H_2O molecules (*e.g.*, $n_w > \sim 10^7$). Water may lose its properties as bulk water to get that of a non-aqueous solvent, such as an alcohol (R–O–H) or even an ether (R–O–R) if the highly "self-assembled structure" of bulk water is disturbed in the following causes: (a) the residual water ($c(H_2O) \sim 10^{-3}$ mol dm^{-3}) in organic solvents; (b) aqueous solutions or organic solvent–water mixtures containing salts at high concentrations; (c) nanoscale water droplets in nano-tubes or reversed micellar systems; (d) water on metal electrodes, ion-exchange resins, proteins, organic solvents in the solvent extractions, and glass vessels; (e) water at higher temperatures or under supercritical conditions. Such water can be "reduced" to authentic singular H_2O molecules ["dihydrogen ether," (H)–O–(H)] [28]. Reichardt et al. [29] have concisely interpreted "dihydrogen ether" that, at high salt concentrations [c(salt) > 5 mol dm^{-3}], region C, according to the solvation model of Frank and Wen [30], can be abolished and only regions A and B survive, resulting in an aqueous solvent called "dihydrogen ether." Very recently, we [31] have dissolved precious metals, especially, pure gold in the mixed media between dilute nitric acid and seawater successfully, after discovering [32] the fact that dilute nitric acid indeed possesses the strong oxidation ability when dilute nitric acid contains concentrated salts.

In binary solvents between water and many organic solvents, we [28,33–37] have examined the effects of added salts on the solvolysis (hydrolysis) reaction rates of various organic compounds. Then, for the first time, we have been able to explain successfully the concentrated salt effects on solvolysis reactions of haloalkanes and related compounds without resorting to different types of ion pairs. The exponential increases in solvolysis rates of S_N1 substrates in the presence of concentrated alkali metal (M^+) and alkaline earth metal (M^{2+}) perchlorates have been attributed to the favorable carbocation (R^+) formation through the association (direct "chemical" interaction) between metal cations (M^+ or M^{2+}) and the leaving group anion (X^-) of a substrate (R–X) in the "modified" solvent. However, the solvolysis (hydrolysis) reaction rate of a typical S_N2 substrate is decelerated by the addition of alkali metal or alkaline earth metal perchlorates. The reasons are as follows: (1) the metal cations have no way to give more of the active species for the typical S_N2 substrate; (2) the activity of water, which should attack the substrate, decreases in the presence of the metal perchlorates.

In the present study, as part of our interest in studying medium effects on reactions of toxic organic compounds, we report the effects of an organic solvent, *i.e.*, acetonitrile (MeCN), and various salts on the hydrolysis reaction rate of *p*-nitrophenyl anthranilate in binary MeCN–H_2O solvents of 0–70% (v/v) MeCN containing the buffer solution of pH = 9.18 at 50 °C. In the absence of salts, the pH effects from 8.50 to 10.0 were examined in the mixed solvents, 0–75% (v/v) MeCN. The primary mechanism of the hydrolysis reaction of *p*-nitrophenyl anthranilate is depicted in Scheme 1. Both the molecule of H_2O and the hydroxide ion (OH^-), which is a prominent nucleophilic anion, can attack the carbonyl carbon of the substrate *p*-NPA, and liberate the *p*-nitrophenoxide ion (which is the leaving group). We would not like to discuss the changes in the reaction rate as just the "medium effects" but would like to try differentiating each factor in the influences on the reaction rate.

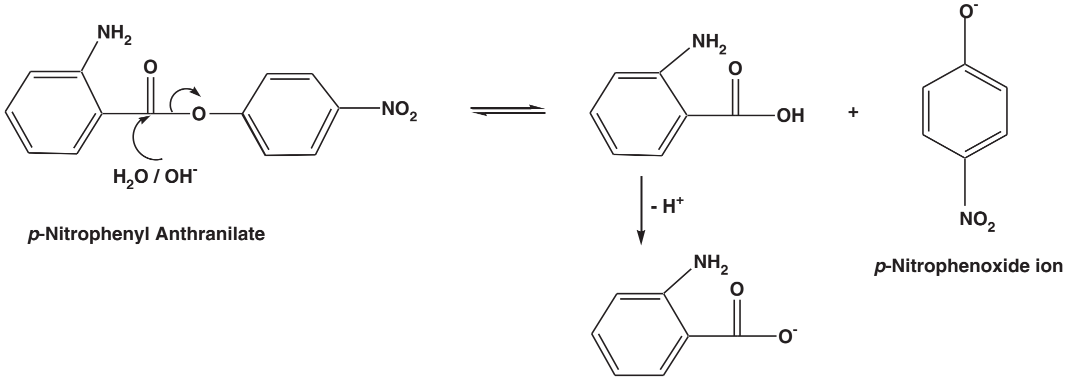
2. Experimental

2.1. Materials and equipment

All chemicals utilized were commercially available and used as received. *p*-Nitrophenyl anthranilate (4-nitrophenyl 2-aminobenzoate, ≥98.0%) and benzoate (>95%) were from TCI and Wako, respectively. Salts of $LiClO_4$ (≥98.0%), Et_4NBr (≥98.0%), Et_4NCl (≥98.0%), NaN_3 (≥98), $(n\text{-}Bu)_4NBr$ (≥98.0%), and $Na_2B_4O_7 \cdot 10H_2O$ (≥99.6) and the co-solvent, acetonitrile (of the GR grade), were from Wako. Other salts of $NaClO_4$ (≥98.0%), Et_4NTsO (tosylate or *p*-toluenesulfonate, ≥97%), and Pr_4NBr (≥98.0%) were from Aldrich. Instead of the commercially available (from Wako) buffer solution, we used the carefully prepared (in laboratory) borate buffer solutions of pH ranging from 8.50 to 10.0 in order to avoid the influences of NaN_3 contained as the stabilizer in the commercial borate buffer. Pure water purified by MilliQ System was used in all the experiments. A Horiba F-51 digital pH meter was used for measuring pH of the buffered solutions. Raman spectra of D_2O containing MeCN were recorded with a Horiba-Jobin Yvon LabRam Spectrograph HR-800 at room temperature (~23 °C). Excitation for the Raman Spectroscopy was provided by a 514.5 nm argon laser.

2.2. Kinetic procedure

Kinetic measurements were performed using a Shimadzu UV–Vis spectrophotometer (Model UV-2550) equipped with a thermostated cell holder whose temperature was controlled within 25 ± 0.1 °C, in a 1.0 cm quartz cuvette. Reaction solutions were prepared by combining the appropriate amounts of water and acetonitrile, the borate buffer of pH = 9.18 (the final concentration of 5.0 mmol dm^{-3}) and salts and then were left to stand for about 30 min in a Taitec constant temperature water bath at 50 ± 0.1 °C in order to reach the thermal equilibrium. Prior to the beginning of the reaction, a stock solution of the substrate (*p*-NPA) (5.0×10^{-3} mol dm^{-3}) in MeCN was prepared since the substrate is sparingly soluble in pure water. Reactions were initiated by transferring 1.0 mL of the stock solution into a reaction vessel (50 mL) to reach the final substrate concentration of 1.0×10^{-4} mol dm^{-3}.



Scheme 1. Schematic representation of hydrolysis reaction mechanism of *p*-NPA.

The samplings of 3–4 mL were carried out from reaction solutions at certain time intervals and the sampled solutions were immediately dipped into an ice water bath. The reaction progress was then followed spectrophotometrically by monitoring the liberation of *p*-nitrophenoxide ion at $\lambda_{max} = ca.$ 400 nm as a function of time. The apparent first order rate constants were obtained from the slopes of plot of ln $(A_\infty - A_t)$ *vs. t*, where A_∞ and A_t are the absorbance values at the reaction final and at time *t*, respectively. All rate constants were obtained from linear plots with correlation coefficients (R^2) of normally 0.999 or more.

3. Results and discussion

3.1. Effects of pH and MeCN contents

At the constant temperature of 50 ± 0.1 °C, the hydrolysis of *p*-nitrophenyl anthranilate (1.0×10^{-4} mol dm^{-3}) has been examined in solutions of 0–75% (v/v) MeCN as co-solvent with water containing the pH buffer ranging from 8.50 to 10.0. The evaluated first order rate constants [log (k/s^{-1})] increase linearly as −4.55, −3.86, −3.56 and −3.18 with increasing pH of the buffer solutions as 8.50, 9.18, 9.50 and 10.0, respectively, in sole aqueous solutions. The increase in the rate acceleration is even about 23 times for pH increment from 8.50 to 10.0. In all the solutions containing MeCN up to 75% (v/v), similar increases in the rate constants are evidenced with increasing pH of the buffer, as shown in Fig. 1. For instance, the log (k/s^{-1}) value in solution containing 20% (v/v) MeCN increase from −4.76 to −3.44 with the pH increase from 8.50 to 10.0.

Increasing contents of the organic solvent (MeCN) cause significant changes in the hydrolysis reaction rate of *p*-nitrophenyl anthranilate. With the constant pH buffer of 9.18, the log (k/s^{-1}) value decrease linearly as −3.87, −3.96, −4.11, −4.21, and −4.41 when the MeCN contents increase as 0, 10, 20, 30 and 50% (v/v), respectively (Fig. 1). The decrease in hydrolysis reaction rate with increasing MeCN contents is mainly ascribed to an alteration of water properties (as discussed in the final section of the present paper) and hence deterioration of water activities in the presence of the organic solvent, MeCN. El-Mallah et al. [4] have noted that MeCN affects the water structure by intercomponent hydrogen bonding due to the basicity difference in the solvent structure. Similarly, Al-Jallal et al. [19] have reported a possible disruption of water tetrahedral structure with increasing MeCN contents.

As the MeCN contents increase to larger than about 50% (v/v), however, the completely reversal trends are observed in the reaction rates, *i.e.*, the hydrolysis rate of *p*-NPA increased again as shown in Fig. 1. For the pH = 9.18 buffer, the log (k/s^{-1}) value varies as −4.41, −4.42, −4.34, and −4.26 in solutions mixed with 50, 60, 70, and 75% (v/v) MeCN, respectively. By the way, the hydrolysis rate constants of *p*-nitrophenyl benzoate also give a similar minimum at about 50% (v/v) MeCN with pH = 8.5 and 9.18 at 40 or 50 °C. The appearance of these minima can be attributed mainly to an increase in the OH^- activity due to the increase in dehydration of OH^- by progressive addition of MeCN. Similar increases in hydrolysis rate constants with increasing contents of organic solvents have been reported by Gomez-Tagle et al. [17] for bis(*p*-nitrophenyl) phosphate.

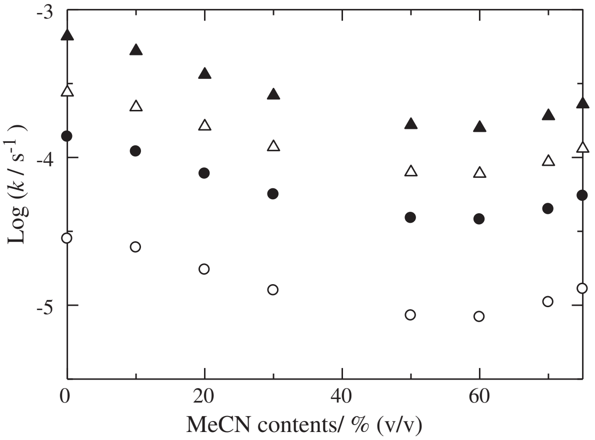


Fig. 1. Changes in log (k/s^{-1}) of *p*-NPA hydrolysis with MeCN contents in aqueous borate buffer solutions of various pH values at 50 ± 0.1 °C: (○) 8.50; (●) 9.18; (△) 9.50; (▲) 10.0.

We may mention that the pK_a value of boric acid increases monotonously as 9.24, 9.57, 10.40, 10.81, 11.25, and 11.84 for 0, 10, 30, 40, 50, and 70% (w/w) MeCN in water at 25 °C [38]. The apparent pH values, by the pH meter measurements after the reaction completion, were found to increase just linearly from 9.23 to 11.23 with increasing MeCN contents up to 75% (v/v).

3.2. Influences of metal perchlorates on the hydrolysis rate

The changes in the hydrolysis reaction rate constant, log (k/s^{-1}), of *p*-nitrophenyl anthranilate were examined in the presence of 0.0–1.0 mol dm^{-3} added alkali metal perchlorate salts ($LiClO_4$ and $NaClO_4$) in buffer solutions of pH = 9.18 mixed with 0–70% (v/v) MeCN at 50 °C. Fig. 2 shows that the log (k/s^{-1}) value decreases linearly with increasing $LiClO_4$ concentration in solutions containing no MeCN. However, the linear curve is altered to concave curves as MeCN contents increase. We have to just note that the log (k/s^{-1}) value without salt in the 70% (v/v) MeCN solvent is larger than that in the 50% (v/v) MeCN solvent (*cf.* Fig. 1 and Table 1). The hydrolysis rate of *p*-NPA decelerates as the concentration of $LiClO_4$ and/or contents of MeCN increase (with the above exception).

The rate deceleration caused by the Na^+ salt is slightly smaller than that of the Li^+ salt (*cf.* Table 1). This is in agreement with their respective crystal ionic sizes [39] and the ability to be hydrated by water molecules. As the hydrolysis of *p*-NPA must be an S_N2 type reaction, the addition of these neutral metal perchlorate salts may cause the hydrolysis rate to decelerate, which may be due to two interdependent reasons: strong solvation of Li^+ and Na^+ ions with H_2O molecules (the prominent molecules responsible to attack the substrate to initiate the hydrolysis reaction) and/or distortion of water structure (which leads to distraction of the water activity) in the presence of these added salts and MeCN. In the presence of salts in high concentrations, bulk water molecules are consumed for hydrating the ions, therefore, the bulk water region in solution should be reduced [27].

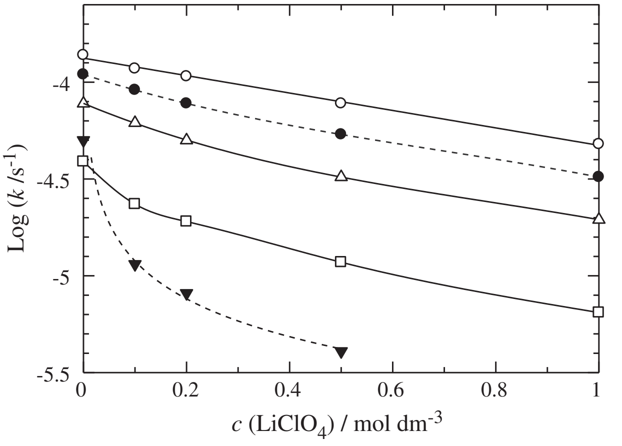


Fig. 2. Changes in log (k/s^{-1}) of *p*-NPA hydrolysis with $LiClO_4$ concentrations in aqueous borate buffer solutions of pH = 9.18 containing MeCN at 50 ± 0.1 °C: (○) 0; (●) 10; (△) 20; (□) 50; (▼) 70% (v/v) MeCN.

Table 1
Log (k/s^{-1}) values for the hydrolysis rate of 1.0×10^{-4} mol dm^{-3} of p-NPA in the presence of added metal perchlorate salts in solutions containing the pH buffer of 9.18 and MeCN at 50 ± 0.1 °C.

Salts	MeCN contents/% (v/v)	c(salt)/mol dm^{-3}				
		0	0.10	0.20	0.50	1.0
$LiClO_4$	0	−3.87	−3.93	−3.97	−4.11	−4.32
	10	−3.96	−4.04	−4.11	−4.27	−4.49
	20	−4.11	−4.21	−4.30	−4.49	−4.72
	50	−4.41	−4.63	−4.72	−4.93	−5.19
	70	−4.34	−4.94	−5.09	−5.39	–
$NaClO_4$	0	(−3.87)	−3.88	−3.95	−4.08	−4.24
	20	(−4.11)	−4.17	−4.24	−4.40	−4.60
	50	(−4.41)	−4.58	−4.69	−4.88	−5.11
	70	(−4.34)	−4.76	−4.91	−5.13	−5.41

3.3. Influences of NaN_3 and non-metallic salts on the hydrolysis rate

On the hydrolysis rate of p-NPA, the influence of various kinds and concentrations of salts from 0.0 to 1.0 mol dm^{-3} was examined in 0.0–70% (v/v) MeCN solutions containing the pH = 9.18 buffer. The log (k/s^{-1}) value is greatly affected by the added salts of all kinds used in this study: the salts of NaN_3, Et_4NCl, Et_4NBr, Et_4NTsO, Pr_4NBr, and (n-Bu)$_4$NBr. Fig. 3 shows that NaN_3 causes the remarkable acceleration even at lower concentrations of the salt (≤0.30 mol dm^{-3}), especially in the solution without MeCN. Compared to the system containing no added salt, the addition of 0.10 mol dm^{-3} NaN_3 causes an acceleration by three times. The hydrolysis rate is too fast to be evaluated in the presence of ≥0.50 mol dm^{-3} NaN_3.

The remarkable acceleration in the presence of NaN_3 is in good agreement with strong nucleophilicity of the N_3^- ion. In addition to the OH^- ion (the prominent nucleophile), the N_3^- ion, being a strong nucleophile, can attack the carbonyl carbon of the p-NPA substrate and liberate the p-nitrophenoxide ion significantly. Edwards and Pearson [40] have reported the following overall nucleophilicity order for S_N2 mechanisms in protic media as $RS^- > ArS^- > I^- > CN^- > OH^- > N_3^- > Br^- > ArO^- > Cl^- >$ pyridine $> AcO^- > H_2O$. However, the rate acceleration observed is not uniform in each solution: the slope of Δlog (k/s^{-1}) *vs.* Δc(NaN_3) [0–0.1 or 0.2 mol dm^{-3}] decrease as 4.70, 3.20, 2.30 and 1.80 in solutions containing 0, 20, 50, and 70% (v/v) MeCN contents, respectively (*cf.*, Figs. 3 and 7). The influence of NaN_3 becomes gradually weaker with increasing MeCN contents probably because the activity of N_3^- is reduced by the association of $Na^+N_3^-$ in the media of which permittivity [4] and solvation ability [41,42] are certainly decreased. We have to stress that true Gutmann's donor number, DN for bulk water is ca. 40 [42] and not the original value of 18, this value has been evaluated for isolated water molecules dissolved in 1,2-dichloroethane [41].

Fig. 4 shows the influences of a non-metallic salt, Et_4NBr, on log (k/s^{-1}) in buffer solutions containing 0–70% (v/v) MeCN, *cf.* Table 2. Generally speaking, the hydrolysis rate of p-NPA increases with increasing Et_4NBr concentration. The influence of Et_4NBr is rather weak in solutions containing smaller proportions of MeCN. However, its effect prominently becomes stronger as the MeCN contents increase. The slope of Δlog (k/s^{-1}) *vs.* Δc (Et_4NBr) is 0.17, 0.30, 0.71, and 1.35 for solutions containing 0, 20, 50, and 70% (v/v) MeCN, respectively. Even though the Br^- ion is a good nucleophile, its ability to attack the carbonyl carbon of the substrate may be hindered with the strong hydration by water in solutions containing lower MeCN contents.

However, with increasing MeCN contents, particularly ≥50% (v/v) MeCN, the Br^- ion may be more free from the solvation (hydration) since the water activities should decrease remarkably in the presence of both large proportions of MeCN and the Et_4NBr salt. Hence, the steep rate acceleration by Et_4NBr can be observed in solutions of higher MeCN contents. The salt Et_4NCl also gives the rate acceleration but much weaker than Et_4NBr. The weaker effect of Cl^-, compared to that of Br^-, in solutions of lower MeCN contents is reasonable because of the weaker nucleophilicity of Cl^- than that of Br^- in protic media [40]. We may mention that the phase separation kept us from evaluating the rate constants in solutions containing both ≥50% (v/v) MeCN and ≥0.50 mol dm^{-3} Et_4NCl (*cf.* Table 2). The phase separation phenomena of the binary MeCN–H_2O mixtures by the addition of chloride salts have been reported [43].

Another salt, Et_4NTsO, gives somehow a strange effect on the hydrolysis of p-NPA, especially, in solutions of higher MeCN contents. The nucleophilicity of the tosylate ion should be very weak. In lower MeCN contents, as expected, the log (k/s^{-1}) is not significantly affected (*cf.* Table 2), and even slightly decreases. However, unexpected increases in reaction rates are observed with increasing Et_4NTsO concentration in ≥50% (v/v) MeCN media. Now that the nucleophilicity of the tosylate ion is small, we may attribute the unexpected acceleration to an activity increase of OH^- brought by the distortion of water structure with the addition of the very bulky salt, Et_4NTsO.

3.4. Cooperative effects of salts and MeCN

Fig. 5 is a graphical illustration for the changes in the hydrolysis rate of p-NPA hydrolysis with the added tetraethylammonium (Et_4NCl and Et_4NBr) salts, (n-Bu)$_4$NBr, NaN_3, and $LiClO_4$ in no MeCN media at

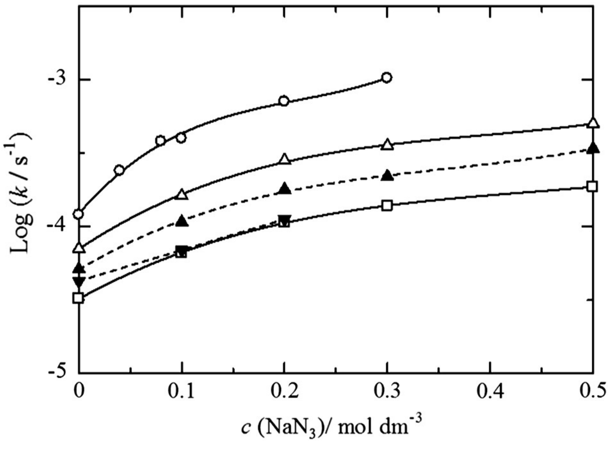


Fig. 3. Changes in log (k/s^{-1}) of p-NPA hydrolysis with NaN_3 concentrations in aqueous borate buffer solutions of pH = 9.18 containing MeCN at 50 ± 0.1 °C: (○) 0; (△) 20; (▲) 30; (□) 50; (▼) 70% (v/v) MeCN.

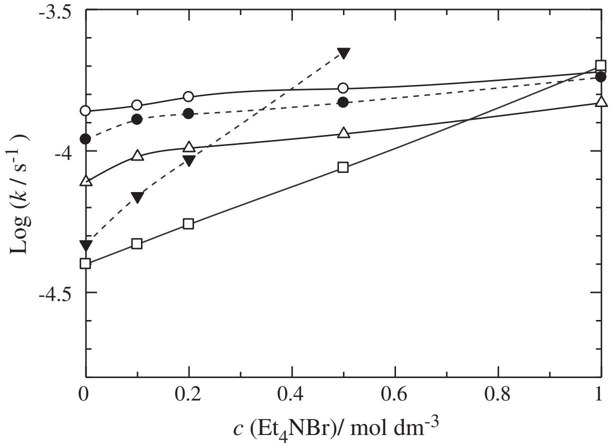


Fig. 4. Changes in log (k/s—^{1}) of p-NPA hydrolysis with Et_4NBr concentrations in pH = 9.18 aqueous buffer solutions containing MeCN at 50 ± 0.1 °C: (○) 0; (●) 10; (△) 20; (□) 50; (▼) 70% (v/v) MeCN.

Table 2
Log (k/s^{-1}) values for the hydrolysis rate of 1.0 × 10^{-4} mol dm^{-3} of *p*-NPA in the presence of various salts in solutions containing the pH buffer of 9.18 and MeCN at 50 ± 0.1 °C.

Salts	MeCN contents/% (v/v)	c(salt)/mol dm^{-3}					
		0	0.10	0.20	0.30	0.50	1.0
NaN_3	0	(−3.87)	−3.40	−3.15	−2.99	–	–
	20	(−4.11)	−3.79	−3.55	−3.45	−3.30	–
	30	(−4.28)	−3.97	−3.75	−3.66	−3.47	–
	50	(−4.41)	−4.18	−3.97	−3.86	−3.73	–
	70	(−4.34)	−4.16	−3.95	–	–	–
Et_4NCl	0	(−3.87)	−3.84	−3.83	–	−3.75	−3.63
	20	(−4.11)	−4.09	−4.08	–	−4.01	−3.95
	50	(−4.41)	−4.39	−4.33	–	–	–
	70	(−4.34)	−4.32	−4.28	–	–	–
Et_4NBr	0	(−3.87)	−3.84	−3.81	–	−3.78	−3.73
	10	(−3.96)	−3.89	−3.87	–	−3.83	−3.74
	20	(−4.11)	−4.02	−3.99	–	−3.94	−3.83
	50	(−4.41)	−4.33	−4.26	–	−4.06	−3.70
	70	(−4.34)	−4.16	−4.03	–	−3.65	–
Et_4NTsO	0	(−3.87)	−3.92	−3.95	–	−4.01	−4.04
	20	(−4.11)	−4.15	−4.14	–	−4.20	−4.15
	30	(−4.28)	−4.29	−4.31	–	−4.29	−4.13
	50	(−4.41)	−4.39	−4.33	–	−4.16	−3.57
	70	(−4.34)	−4.20	−4.04	−3.91	–	–
Pr_4NBr	0	(−3.87)	−3.82	−3.80	–	−3.80	−3.81
	20	(−4.11)	−4.00	−4.00	–	−3.99	−3.88
	50	(−4.41)	−4.23	−4.16	–	−3.95	−3.44
	70	(−4.34)	−4.10	−3.93	−3.82	–	–
(n-Bu)$_4$NBr	0	(−3.87)	−3.80	−3.85	–	−3.98	−4.07
	20	(−4.11)	−4.10	−4.13	–	−4.19	−4.11
	30	(−4.28)	−4.20	−4.20	–	−4.19	−3.92
	50	(−4.41)	−4.33	−4.27	–	−4.06	−3.41
	70	(−4.34)	−4.08	−3.91	−3.84	–	–

50 °C. Here, we can clearly notice that all the NaN_3, Et_4NCl, and Et_4NBr salts accelerate the hydrolysis rate with their respective concentrations. As mentioned above, NaN_3 gives the influence significantly stronger than Et_4NBr or Et_4NCl. In the presence of 0.0 to 1.0 mol dm^{-3} (n-Bu)$_4$NBr (except for 0.10 mol dm^{-3}), the log (k/s^{-1}) value decreases from −3.87 to −4.07. The addition of Pr_4NBr causes the log (k/s^{-1}) value to increase slightly from −3.87 to −3.81 for 0.0 to 1.0 mol dm^{-3} Pr_4NBr. This is in agreement with these tetraalkylammonium cation sizes [39] and their distortion effects on water properties/activities. The (n-Bu)$_4$N$^+$ cation is larger in size than Pr_4N^+, and hence is expected to cause more remarkable distraction in water property. We [32] have discussed that cations such as Et_4N^+, Pr_4N^+, and (n-Bu)$_4$N$^+$ are, potentially, water “structure breakers” and their effects on the possible water disruption should increase in the order of $Et_4N^+ < Pr_4N^+ <$ (n-Bu)$_4$N$^+$.

In 20% (v/v) MeCN media, the rate acceleration by NaN_3 is found to be weaker than that in no MeCN. The Et_4NBr salt shows a stronger effect than Et_4NCl. Generally, the rate acceleration decreased in the order of $NaN_3 > Et_4NBr > Et_4NCl$ in solutions of 20% (v/v) MeCN. The salt of (n-Bu)$_4$NBr remains still in the salt group of rate deceleration, not so distinct as $LiClO_4$ and $NaClO_4$.

Fig. 6 shows the changes of log (k/s^{-1}) in solutions of 50% (v/v) MeCN in the presence of various salts. The most remarkable event in the 50% (v/v) MeCN media is the fact that the hydrolysis rate constant is accelerated by (n-Bu)$_4$NBr. Whereas, this bulky salt causes the deceleration effects in zero and 20% (v/v) MeCN media. The rate acceleration caused by the increasing concentration of Pr_4NBr or (n-Bu)$_4$NBr is significantly enhanced with increasing MeCN contents. For instance, the log (k/s^{-1}) value in the presence of 1.0 mol dm^{-3} of (n-Bu)$_4$NBr in 50% (v/v) MeCN media is as high as −3.41, which is much larger than −3.70 for 1.0 mol dm^{-3} Et_4NBr. The presence of bulky salts, such as Pr_4NBr and (n-Bu)$_4$NBr, in the solution containing the larger volume of an organic solvent can destroy the bulk water structure largely, *cf.* ref. [34]. Hence, the hydrolysis reactions in such solutions should be quite different from the corresponding reactions in dilute aqueous media.

For the solutions containing salts up to 0.50 mol dm^{-3}, the rate accelerations reduce in the order of $NaN_3 >$ (n-Bu)$_4$NBr ~ $Et_4NBr > Et_4NCl$ in 50% (v/v) MeCN media. At 1.0 mol dm^{-3}, however, the influence of (n-Bu)$_4$NBr is superior to that of Et_4NBr, which is ascribed to mainly the destruction of water properties to a greater extent and/or the increase in nucleophilicity of the Br^- ion (and also the OH^- ion).

Fig. 7 shows the changes in the slopes of Δlog (k/s^{-1}) / Δc (salt) *vs.* MeCN contents [% (v/v)] in the presence of various salts. Here we can clearly notice that the acceleration by NaN_3 (of lower concentrations, ≤0.20 mol dm^{-3}) is extremely larger than any other salts used, even though, its effect become weaker as the MeCN contents increase. On the other hand, the effects caused by Et_4NBr and (n-Bu)$_4$NBr salts are enhanced with increasing MeCN contents.

We may decide that the small acceleration effect by Et_4NCl is not significantly altered, *i.e.*, a rather uniform effect, although its effect at higher concentrations (≥0.50 mol dm^{-3}) in ≥50% (v/v) MeCN media cannot be evaluated because of the phase separation (*vide supra*). In 70% (v/v) MeCN media, as the general rule, the rate acceleration caused by added salts is in the order of NaN_3 ~ (n-Bu)$_4$NBr $> Et_4NBr > Et_4NCl$ and the deceleration by $LiClO_4$ (or $NaClO_4$). The ClO_4^- ion has no nucleophilicity, therefore, $LiClO_4$ (or $NaClO_4$) cannot assist the hydrolysis of this S_N2 substrate. The rate deceleration becomes

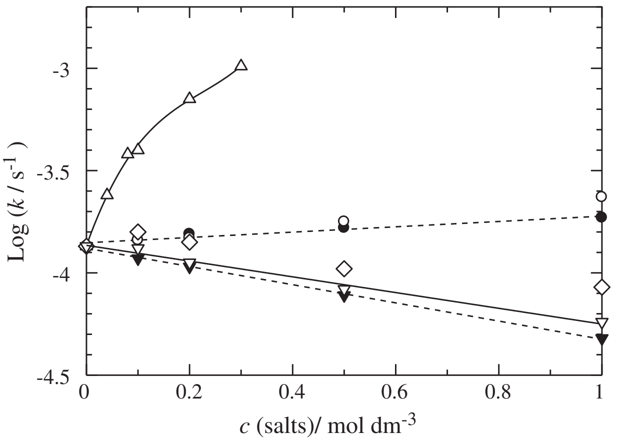


Fig. 5. Changes in log (k/s^{-1}) of *p*-NPA hydrolysis with salt concentrations in pH = 9.18 aqueous buffer solutions of containing no MeCN at 50 ± 0.1 °C: (△) NaN_3; (○) Et_4NCl; (●) Et_4NBr; (◊) (n-Bu)$_4$NBr; (▼) $LiClO_4$; (▽) $NaClO_4$.

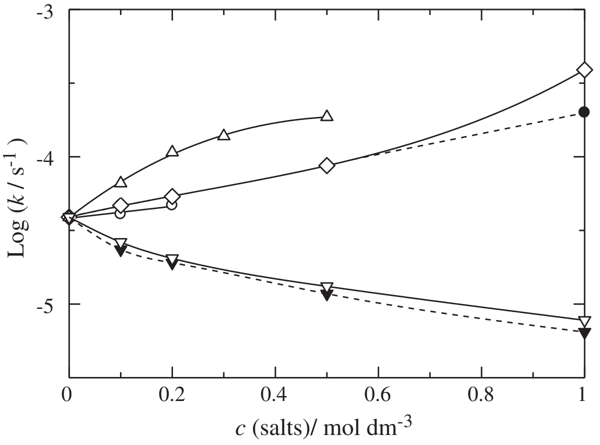


Fig. 6. Changes in log (k/s^{-1}) of *p*-NPA hydrolysis with salt concentrations in pH = 9.18 aqueous buffer solutions containing 50% (v/v) MeCN at 50 ± 0.1 °C: (△) NaN_3; (○) Et_4NCl; (●) Et_4NBr; (◊) (n-Bu)$_4$NBr; (▼) $LiClO_4$; (▽) $NaClO_4$.

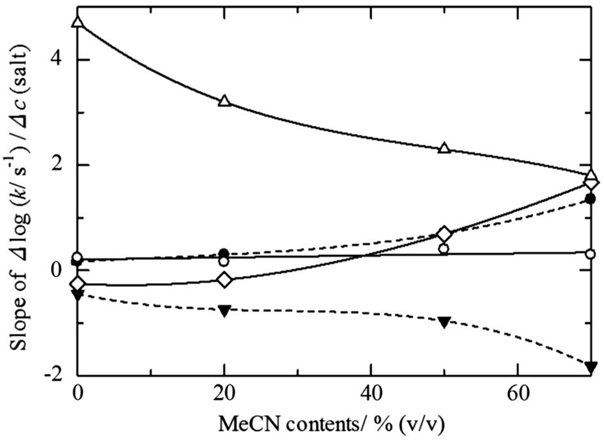


Fig. 7. Changes in slopes of $\Delta\log(k/\text{s}^{-1})/\Delta c$ (salt) *vs.* MeCN contents for hydrolysis of *p*-NPA in aqueous buffer solutions of pH = 9.18 at 50 ± 0.1 °C containing salts: (Δ) NaN_3; (○) Et_4NCl; (●) Et_4NBr; (◊) $(n\text{-}Bu)_4NBr$; (▼) $LiClO_4$.

remarkably as both its salt concentration and the MeCN contents increase because more water molecules are involved in solvating Li^+ (or Na^+) ions and the bulk water properties should be reduced.

3.5. Temperature dependence

Fig. 8 shows the Arrhenius plots of log (k/s^{-1}) in binary MeCN-H_2O mixed solvents (buffered with pH = 9.18) of 0 - 30% (v/v) MeCN. The relationship between log (k/s^{-1}) and T^{-1} is linear over the temperature range of 35 – 60 °C (or 65 °C) for 10, 20, and 30% (v/v) MeCN, whereas the relation gives convex curves at lower temperatures, *i.e.*, < 50 and < 40 °C for 0.0 and 5.0% (v/v) MeCN, respectively. The activation energy (E_a) values are evaluated from the straight part to be 91.5, 93.8, 94.6, 99.6, and 102.1 kJ mol^{-1} for the 0.0, 5.0, 10, 20, and 30% (v/v) MeCN media. We can notice that the log (k/s^{-1}) values of *p*-NPA give a maximum at 5.0 or 10% (v/v) MeCN for 40 or 35 °C, respectively, while the rate constant decreases just monotonously with increasing MeCN contents (in 0.0, 5.0, 10, 20, and 30% media) at the higher temperatures, *e.g.* 60 °C. In an additional study, we have examined the hydrolysis rate of *p*-nitrophenyl benzoate in the binary MeCN-H_2O media. The log (k/s^{-1}) values of *p*-nitrophenyl benzoate give a maximum at about 10% (v/v) MeCN (buffered with pH = 8.50 and 9.18) at 40 or 50 °C.

Fig. 9 shows the Arrhenius plots of log (k/s^{-1}) in 50% (v/v) MeCN–H_2O buffered solution (with pH = 9.18) in the presence of various salts. All the 50% (v/v) MeCN–H_2O solution systems give the good linearity from 35 to 60 °C, resulting in the activation energy (E_a) of 107.0, 98.8, 84.2, and 104.2 kJ mol^{-1} for no salt, $LiClO_4$, NaN_3, and Et_4NBr of 0.2 mol dm^{-3}, respectively. These large values of the activation energy in the systems with added salts suggest that the hydrolysis reaction of the substrate is just of temperature dependence.

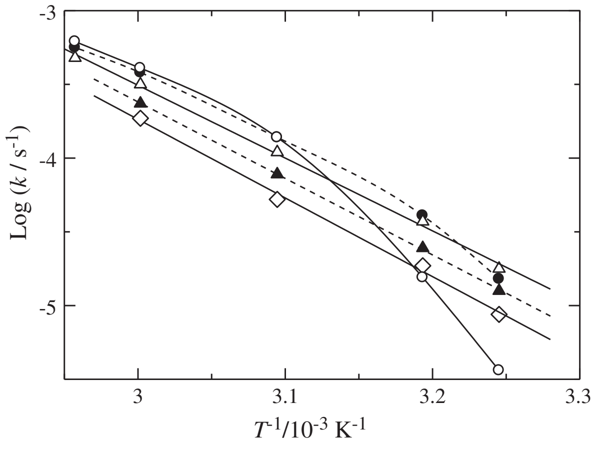


Fig. 8. Arrhenius plots of log (k/s^{-1}) in binary MeCN–H_2O mixed solvents (buffered with pH = 9.18) : (○) 0.0; (●) 5.0; (Δ) 10; (▲) 20; (◊) 30% (v/v) MeCN.

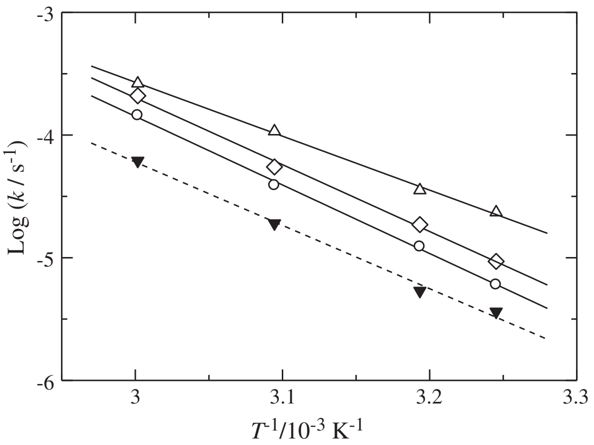


Fig. 9. Arrhenius plots of log (k/s^{-1}) in 50% (v/v) MeCN–H_2O buffered solution (with pH = 9.18) in the presence of various salts: (○) no salt; (▼) 0.20 mol dm^{-3} $LiClO_4$; (Δ) 0.20 mol dm^{-3} NaN_3; (◊) 0.20 mol dm^{-3} Et_4NBr.

3.6. Changes in Raman spectra of water (D_2O) with the addition of MeCN

Raman spectroscopy has been often employed to investigate the dynamical structure of water for a long time [44–46]. It is a technique preferably used for studies of water structure because the proportions of intensities of main OH stretching modes (around 3200 and 3400 cm^{-1}) are thought to reflect well the network of hydrogen bonds as well as its disturbance by the presence of other substances like solutes and organic solvents [34]. Distortion of water structure in the presence of added solvents and salts, or with increasing temperature, has been extensively investigated and reported [33,34,37,47].

Fig. 10 shows the change in Raman spectra of D_2O with increasing MeCN contents [0–90% (v/v)] at room temperature. Pure D_2O gives an OD stretching band with two peaks at around 2380 and 2500 cm^{-1}, which are assigned to strongly hydrogen bonded D_2O and weakly hydrogen-bonded D_2O, respectively [48]. Upon addition of MeCN to D_2O, the peak intensity at around 2500–2600 cm^{-1} increases while the intensity at around 2380 cm^{-1} decreases. The increase in MeCN

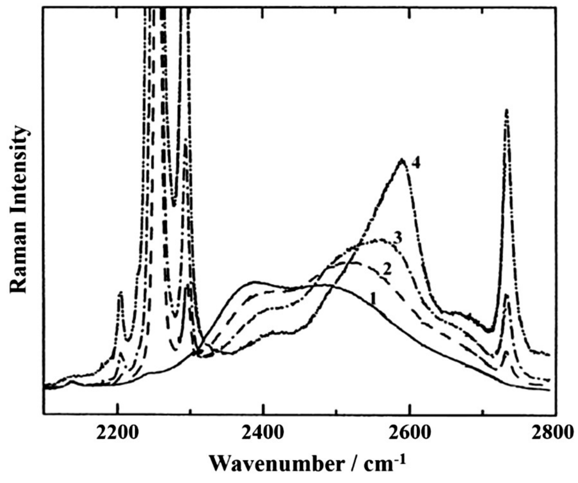


Fig. 10. Changes in Raman spectra of D_2O with increasing MeCN contents: (1) 0; (2) 50; (3) 75; (4) 90% (v/v) MeCN.

contents causes further decrease and increase in the peak intensity (I_1 and I_2) at around 2400 and 2500–2600 cm^{-1}, respectively. The ratios of Raman OD band intensities (I_1/I_2) around 2400 and 2500–2600 cm^{-1} are significantly changed with MeCN contents.

The Raman intensity ratios (I_1/I_2) decrease as 1.03, 0.72, 0.53, and 0.23 with increasing contents of MeCN as 0, 50, 75, and 90% (v/v), respectively, witnessing the distortion of the D_2O bulk structure in the presence of the organic solvent. At the same time, peaks at 2380 and 2500 cm^{-1} shift to higher wavenumbers as the MeCN contents increase. At 90% (v/v) MeCN, the wavenumber of weakly hydrogen bonded D_2O seemed to approach even that of D_2O monomer ($\upsilon_1 = 2671\ cm^{-1}$) in the gas phase [49].

4. Conclusion

The hydrolysis reaction rate of *p*-nitrophenyl anthranilate (*p*-NPA) is greatly influenced by pH, added salts of various kinds and MeCN contents in binary MeCN–H_2O mixed solvents. Increase in MeCN contents up to 50% (v/v) retards the hydrolysis reaction of *p*-NPA, whereas, further increments of MeCN cause the reversal increases in log (k/s^{-1}). Metal perchlorate salts, such as $LiClO_4$ and $NaClO_4$, decelerate the hydrolysis rate in all the media. It is concluded that the significant changes in the hydrolysis rate constant are dependent upon not only the activities of H_2O and OH^- but also the nucleophilicities (toward the carbonyl carbon atom in *p*-NPA) of the anions (N_3^-, Cl^-, Br^-, and TsO^-) from added salts in the “modified” aqueous solution, where the hydrogen bonding structure of the bulk water is distorted by the addition of foreign substances, *i.e.*, the organic solvent and the salts.

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